SECTION II
REMARKS

Regarding the Amendments

By the present Amendment, claim 1 has been amended. Claim 1 is amended solely to include text mistakenly omitted, but not intentionally cancelled from claim 1 in the Listing of the Claims provided in the Preliminary Amendment filed February 1, 2006. No additional amendments are made to the claims.

No new matter within the meaning of 35 U.S.C. §132(a) has been introduced by the foregoing amendments.

The amendments made herein are fully consistent with and supported by the originally-filed disclosure of this application.

Thus, upon entry of the amendments, claims 1-28 will be pending, of which claims 1-15, 21, and 23-28 are withdrawn.

Objection to the Drawings

The examiner has rejected Figs. 8, 10 and 11 as including shading that is indistinguishable between samples listed in the legend. In response, applicants submit two sheets of replacement drawings; both labeled "REPLACEMENT SHEET." The first sheet contains Figs. 8 and 9 and the second sheet contains Figs. 10 and 11. Only objected to Figs. 8, 10 and 11 are amended in these newly submitted pages. As Fig. 9 was originally included on the same sheet as Fig. 8, it is included in the replacement sheet.

As amended, the Figures contain clear distinction among the samples indicated. Withdrawal of the objection is respectfully requested.

Rejection of Claims under 35 U.S.C. §112, second paragraph

Claim 16 was rejected under 35 U.S.C. §112, second paragraph as indefinite for dependence upon claim 1, where the particle diameter is recited as "less than μm." Applicants respectfully

draw the examiner's attention to the amended claims, as set forth above. By the present Response, applicants have amended the claim to include a numerical value of "1" preceding "μm" and have also added the term "comprising" where appropriate.

Support is found for addition of these terms in the original specification and the preliminary amendment filed on December 20, 2005, with the original filing of the application.

In a subsequent preliminary amendment, filed on February 1, 2006, these terms were mistakenly omitted from claim 1. The claim was not amended by that preliminary amendment, as indicated by the status identifier "Previously presented." By the present Response, the terms are added back to claim 1. Claim 1 is presently withdrawn from consideration. Claim 16, presently pending and under examination depends from amended claim 1 and it is clear that the particle diameter is less than 1 μm.

Accordingly, claim 16 is in compliance with eh definiteness requirements of 35 U.S.C. §112, second paragraph and withdrawal of the rejection of claim 16 is respectfully requested.

Rejection of Claims Under 35 U.S.C. §103

Claims 16-20 and 22 are rejected by the examiner under 35 U.S.C. §103 as obvious over U.S. Patent Application Publication No. 2003/0170313 (hereinafter Prokop et al.) in view of U.S. Patent Application Publication No. 2003/0087877 (hereinafter Calias et al.) Applicants respectfully disagree.

Specifically, the examiner alleges that the nanoparticles described in the present invention only differ from the first composition disclosed in the table 1 of Prokop et al. by the presence of Hyaluronic Acid (HA) or its salts as anionic component. Since Calias et al. describe the use of polyanionic polysaccharides such as HA, the examiner considers that it would have been obvious to reach the present invention by replacing the anionic component of Prokop et al. with the salts of HA disclosed in Calias et al.

It is elemental law that in order for an invention to be obvious, the difference between the subject matter of the application and the prior art must be such that the subject matter as a whole would

have been obvious at the time the invention was made to a person of ordinary skill in the art. In order to meet this standard for a proper §103 rejection, all claim limitations must be disclosed or derivable from the cited combination of references, there must be a logical reason to combine the cited references to produce an operable combination and there must be a reasonable expectation of success. (MPEP §2143)

Prokop et al. in view of Calias et al. fail to provide any derivative basis for the claimed invention and, additionally, there would have been no logical reason for one of skill in the art to combine such references. Accordingly, no basis of *prima facie* obviousness of the claimed invention is presented by such cited references.

The examiner alleges that the nanoparticles recited in claim 16 differ from those described in Prokop et al. by the inclusion of a hyaluronic acid salt, as anionic component, which is not mentioned among the anionic polymers described in Prokop et al.

The use of a hyaluronic acid salt in the method of claim 1, by which the nanoparticles of claim 16 are obtained, advantageously provides the nanoparticles with a higher stability. This improved stability can be seen in the examples provided of the application, primarily in Example 4. Figs. 4 and 5, illustrating the results of that Example, show that the nanoparticles preserve their properties for at least one month. By contrast, the nanoparticles disclosed in Prokop et al. are typically stable for 3-5 days [see page 9, end of paragraph 0100] and only show a longer stability (3 weeks) at low temperatures (4°C) and when they are subjected to a crosslinking step, after being obtained and isolated [see example 12], that it is to say, by means of a different and more complex process.

While Prokop et al. state the intention of "making a nanoparticle that is stable in a physiological environment for at least a day" (para. [0029]), that stabiklity is attributed to "the complex structure forming the nanoparticle made by this method increases the stability of the nanoparticle in a physiological environment" (para. [0014]). Prokop et al. do not attribute the stability to the anionic polymer element.

In addition, the person skilled in the art faced with the problem of developing nanoparticles with higher stability than those of Prokop et al. would have not considered the combination of Prokop et al. with Calias et al., since Calias et al. is directed to the preparation of a very different drug release system. Specifically, Calias et al. discuss a bioconjugate comprising a solid biomaterial

over which a therapeutic agent is supported. In fact, the selection of hyaluronic acid in Calias et al. as biomaterial is due to the fact that it presents free carboxyl groups which can be activated and functionalized in order to enable the formation of disulfide bridges with therapeutical agents comprising thiol groups. Accordingly, in Calias et al. the hyaluronic acid confers stability to the therapeutic agent by means of covalent interactions, whereas the nanoparticles of the invention are obtained by electrostatic interactions (ionic gelification process) of their components [see paragraph 0033 of the specification]. Therefore, one of skill in the art, viewing Calias et al. would not have found it obvious that hyaluronic acid could confer a higher stability to a drug release system in the form of nanoparticles and wherein said nanoparticles have been obtained by electrostatic interactions. Therefore, there would have been no logical basis for one of skill in the art to combine Prokop et al. with Calias et al.

As Prokop et al. in view of Calias et al. does not provide any logical basis for the nanoparticles recited in claims 16-20 and 22, Prokop et al. in view of Calias et al. does not render the claimed invention obvious. Accordingly, withdrawal of the rejection of claims 16-20 and 22 under 35 U.S.C. § 103 (a) as being obvious over Prokop et al. in view of Calias et al. is respectfully requested.

CONCLUSION

All of Applicants' pending claims 1-15, 21, and 23-28 are patentably distinguished over the art, and in form and condition for allowance. The Examiner is requested to favorably consider the foregoing and to responsively issue a Notice of Allowance.

The time for responding to the June 23, 2008 Office Action without extension was set at three months, or September 23, 2008. Applicants hereby request a one month extension of time under 37 CFR § 1.136 to extend the deadline for response to October 23, 2008. Payment of the extension fee of $130.00 specified in 37 C.F.R. § 1.17(a)(1), as applicable to large entity, is being paid by on-line credit card payment at the time of EFS submission of this Response. Should any additional fees be required or an overpayment of fees made, please debit or credit our Deposit Account No. 08-3284, as necessary.

If any issues require further resolution, the Examiner is requested to contact the undersigned attorneys at (919) 419-9350 to discuss same.

Respectfully submitted,

Date: October 23, 2008

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Enclosures:
Drawing Replacement Sheets [2 pgs.]

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